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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/870,762	06/06/1997	BRADFORD J. DUFT	226/104US	7328

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Intellectual Property Department
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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	08/870,762	DUFT ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *090506*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendments filed 12/01/06 in response to the non-final Office Action mailed 06/01/06. With this, Applicants have amended the specification and the claims.

Status of Claims

2) Claim 8 has been canceled via the amendment filed 12/01/06.

Claims 1-7 and 9-16 have been amended via the amendment filed 12/01/06.

New claim 17 has been added via the amendment filed 12/01/06.

Claims 1-7 and 9-17 are pending and are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' Information Disclosure Statement filed 09/05/06. The information referred to therein has been considered, except the documents, which have already been considered or cited on a PTO-892, and a signed copy is attached to this Office Action.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Specification

6) The specification is objected to for the following reason(s):

(a) The amendments introduced to the specification via the amendment filed 09/30/05 introduces brackets while reciting '[SEQ ID NO: ..]'. It is unclear whether the brackets are

intended to delete the recited 'SEQ ID NO: ...', or intended to appear in the printed patent. If the latter is intended, it is suggested that Applicants replace the limitation with the limitation --(SEQ ID NO: ...)--.

(b) The second full sentence on page 7 of the substitute specification is incorrect. The sentence states as follows [Emphasis in original]:

> Since the work described by the inventors herein with regard to the effect of amylin and amylin agonists to decrease body weight in humans, several publications have reported that infusion of amylin can cause anorexia in rats. See Arnelo et al. Am. J. Physiol. 40:R1654-R1659 (1996); Arnelo et al. Scan. J. Gastroenterol., 31:83-89 (1966).

The year of publication of the second Arnelo et al. reference appears to be incorrect.

Objection(s) Withdrawn

7) The objection to the specification made in paragraph 9 of the Office Action mailed 6/01/06 is withdrawn in light of Applicants' amendments.

Objection(s) Maintained

8) The objection to the specification made in paragraph 10(a) of the Office Action mailed 06/01/06 is maintained for reasons set forth therein and herebelow.

Applicants contend that the paragraphs objected to are all taken from the contents of the patent application incorporated by reference on page 10 of the substitute specification or page 14 of the original specification. Applicants acknowledge that the specification's direct reference is to the amylin agonist analogs in the referenced application and that this is specifically indicative that material related to the amylin agonist analogs is to be incorporated. Applicants state that Examples 9-20 in particular provide information on the preparation of the specific analogs that are listed in originally filed Table II.

Applicants' arguments have been carefully considered, but are not persuasive. It is noted that Applicants have deleted the paragraph immediately preceding paragraph 9. Table II of the instant application depicts the receptor binding assay and the soleus muscle assay results for SEQ ID NO: 4-15, but does not describe the peptide synthetic 'methods of preparing' SEQ ID NO: 4-15, SEQ ID NO: 24 and SEQ ID NO: 25. Table II of the instant application does not even make a mention of SEQ ID NO: 24 and 25. The objection stands.

Rejection(s) Moot

9) The rejection of claim 8 made in paragraph 12 of the Office Action mailed 05/30/02 and made/maintained in paragraph 28 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

10) The rejection of dependent claim 8 made in paragraph 30 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

11) The rejection of claim 8 made in paragraph 39 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claim.

12) The rejection of claim 8 made in paragraph 42 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claim.

13) The rejection of claim 1 and those dependent therefrom and of claim 16 made in paragraph 43 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn. A modified rejection is set forth herein below to cover the claims as amended currently.

14) The rejection of claim 8 made in paragraph 44(f) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

15) The rejection of claim 8 made in paragraph 47 of the Office Action mailed 06/01/06 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Maintained

16) The provisional rejection of claims 1-6 made in paragraph 10 of the Office Action mailed 11/13/00 under the judicially created doctrine of double patenting over the claims of the pending

application, SN 09/445,517, and maintained in paragraph 9 of the Office Action mailed 05/30/02 and maintained in paragraph 27 of the Office Action mailed 06/01/06, is still maintained for reasons set forth therein. Applicants state that a terminal disclaimer will be filed upon withdrawal of all other outstanding rejections.

17) The provisional rejection of claims 7, 13, 14 and 16 made in paragraph 37 of the Office Action mailed 06/01/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 33 of the co-pending application 09/445,517, is maintained for reasons set forth therein. Applicants' statement that they are willing to consider submitting a terminal disclaimer in the present application with regard to the '517 application should this application issue as a patent prior to the present application has been noted.

18) The provisional rejection of claims 7, 14 and 16 made in paragraph 38 of the Office Action mailed 06/01/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of the co-pending application, 10/851,574, is maintained for reasons set forth therein. Applicants' statement that they are willing to consider submitting a terminal disclaimer in the present application with regard to the '574 application should this application issue as a patent prior to the present application has been noted.

19) The rejection of claim 14 made in paragraph 40 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is maintained for reasons set forth therein and herebelow.

Applicants contend that the substitute specification at the paragraph beginning at line 20 of page 20 and the original specification at the paragraph beginning at line 14 of page 24 describe that 'the amylin and amylin agonists may form salts that are pharmaceutically acceptable'. Applicants submit that many of the salts described in the specification, such as acetate, hydrochloride and trifluoroacetate salts, are known in the art to be pharmaceutically acceptable.

Applicants' arguments have been carefully considered, but are not persuasive. The paragraph beginning at line 14 of page 24 of the specification as originally filed and the paragraph beginning at line 20 of page 20 of the substitute specification does not identify or distinguish any of the salts to be 'pharmaceutically acceptable' or pharmaceutically non-acceptable. The support for a

newly added narrower limitation must come from Applicants' specification as filed. The rejection stands.

Rejection(s) Withdrawn

20) The rejection of claims 1-6 and 9-13 made in paragraph 12 of the Office Action mailed 05/30/02 and made/maintained in paragraph 28 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claims.

21) The rejection of claims 1, 7 and 16 made in paragraph 14(a) of the Office Action mailed 05/30/02 and made/maintained in paragraph 29 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

22) The rejection of dependent claims 2-6, 9-13 and 15 made in paragraph 14(b) of the Office Action mailed 05/30/02 and made/maintained in paragraph 30 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim(s).

23) The rejection of claim 14 made in paragraph 33 of the Office Action mailed 06/01/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 64 and 68 of US patent 6,956,026 ('026, filed 01/07/1997), is withdrawn in light of Applicants' amendment to the claim.

24) The rejection of claims 7 and 14 made in paragraph 34 of the Office Action mailed 06/01/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 85 of the U.S. patent 5,739,106 (Rink *et al.*), is withdrawn in light of Applicants' amendment to the claims.

25) The rejection of claims 7, 13, 14 and 16 made in paragraph 35 of the Office Action mailed 06/01/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract), is withdrawn. A modified/new

rejection is set forth below to reject the claims as amended currently. Applicants' arguments with respect to the rejection have been considered but are moot in view of the modified/new rejection set forth below. Applicants' acknowledgment that obesity is common among those with diabetes has been noted.

26) The rejection of claims 7, 13, 14 and 16 made in paragraph 36 of the Office Action mailed 06/01/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract) and Rink *et al.* (US 5,739,106) ('106), is withdrawn. A modified/new rejection is set forth below to reject the claims as amended currently. Applicants' arguments with respect to the rejection have been considered but are moot in view of the modified/new rejection set forth below. Applicants' acknowledgment that obesity is common among those with diabetes has been noted.

27) The rejection of claims 9-13 made in paragraph 39 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claims.

28) The rejection of claim 15 made in paragraph 41 of the Office Action mailed 06/01/06 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claim and/or the base claim.

29) The rejection of claims 7 and 16 made in paragraph 44(a) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

30) The rejection of claims 2-6 and 9-13 made in paragraph 44(b) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

31) The rejection of claim 3 made in paragraph 44(c) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

32) The rejection of claim 15 made in paragraph 44(d) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

33) The rejection of claims 9-13 made in paragraph 44(e) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

34) The rejection of claims 3, 5, 6, 9, 10 and 15 made in paragraph 44(f) of the Office Action mailed 06/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

35) The rejection of claims 7, 14 and 16 made in paragraph 46 of the Office Action mailed 06/01/06 under 35 U.S.C § 102(e)(2) as being anticipated by Beeley *et al.* (US 6,956,026), is withdrawn in light of Applicants' amendment to the base claim.

36) The rejection of claims 1-7, 9 and 11-16 made in paragraph 47 of the Office Action mailed 06/01/06 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996), is withdrawn in light of Applicants' amendments to the claims and/or the base claims. A modified/new rejection is set forth herein below to cover the claims as amended. Applicants' arguments with respect to the rejection have been considered but are moot in view of the modified/new rejection set forth below.

37) The rejection of claims 1-7, 9-14 and 16 made in paragraph 48 of the Office Action mailed 06/01/06 under 35 U.S.C § 102(a) as being anticipated by Kolterman *et al.* (WO 96/40220, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. A modified/new rejection is set forth herein below to cover the claims as amended. Applicants' arguments with respect to the rejection have been considered but are moot in view of the modified/new rejection set forth below. Applicants' acknowledgment that obesity is indeed a common characteristic of patients with type II diabetes mellitus has been noted.

Double Patenting Rejection(s)

38) Claims 7, 14, 16 and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* ('411, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract). Although the conflicting claims are not identical, they are not patentably distinct from each other. The method of treatment claimed in claims 34 and 35 of the '411 patent is for the treatment of diabetes mellitus in a mammal comprising the administration to said mammal of a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1). The portion of the disclosure of the '411 patent at lines 45-53 in column 7 supporting the limitation mammal does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. The amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, about 0.1 milligrams to about 1 milligram per day, or 300 micrograms per dose, falls in the range disclosed in the '411 patent. The portion of the disclosure of the U.S. patent '411 at lines 9-14 of column 3 describes that the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus and that the administration is of amylin agonist analogue *alone*. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev, at least 80-90% of the diabetic patients used in the method disclosed in the '411 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '411 patent comprising the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist ^{25,28,29}Pro-human amylin to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims and the amount administered are the same, the method of the '411 patent is expected to bring about a therapeutic effect against intrinsic obesity in the treated diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

39) Claims 7, 14 and 16 are rejected under the judicially created doctrine of obviousness-type

double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record) and Rink *et al.* (US 5,739,106, already of record) ('106). Although the conflicting claims are not identical, they are not patentably distinct from each other. The limitation 'consisting essentially of' in claim 16 does not exclude the presence of insulin in the recited composition. The method claimed in claims 11 and 13 of the US patent 5,321,008 is for the treatment of diabetes mellitus in an insulin-requiring human comprising the administration to said human of a therapeutically effective amount of a calcitonin alone, or calicitonin and insulin. Claim 11 of the '008 patent is directed to the method of administering a therapeutically effective amount of the amylin agonist calcitonin to an insulin-requiring human with diabetes mellitus. The portion of the disclosure of the '008 patent at lines 14-17 in column 5 supporting the limitation 'human' expressly includes a human who suffers from Type 1 or Type 2 diabetes mellitus. The portion of the disclosure of the '008 patent at first full paragraph in column 13 supporting the limitation 'therapeutically effective amount' includes the typical dosage units of about 0.1 to 1 mg of calcitonin. The amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls in this range disclosed in the '008 patent. The portion of the '008 patent that supports the composition in column 12 includes the presence of a pharmaceutically acceptable carrier in the composition and subcutaneous administration. See lines 8-11 and 49-54 in column 12. Given the art-known fact that calcitonin is an amylin agonist as taught at lines 34 and 35 of column 3 of the '008 patent and at line 4 of column 16 of Rink *et al.* ('106), and the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev, at least 80-90% of the type 2 diabetic patients used in the method disclosed in the '008 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to a diabetic human anticipates the instant claims. Given that the method step of the '008 patent and the instant claims are the same and the amount administered are the same, the method of the '008 patent is expected to bring about a therapeutic effect against the intrinsic obesity in the treated

type 2 diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

40) Claim 14 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 14, as amended, includes the limitation: a human subject 'in need thereof'..... pharmaceutically acceptable salts thereof, 'wherein said compound is administered in an amount effective to treat obesity and wherein said compound is not administered in conjunction with another obesity relief agent'. Applicants state that the support for the amendment can be found throughout the specification, the claims as originally filed, the abstract, and at lines 8 and 9 of page 9 of the substitute specification. However, this part of the specification does not describe a method of treating obesity in a human subject in need thereof comprising administering to said subject 'a pharmaceutically acceptable salt' of an amylin or an amylin agonist which is administered in an amount effective to treat obesity and which is 'not administered in conjunction with another obesity relief agent. Therefore, the above-identified limitation in the new claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

41) Claims 9 and 10 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of

the claimed invention. This is a new matter rejection.

Claim 9, as amended, includes the limitations: 'the composition is administered QID'. Claim 10, as amended, includes the limitation: 'the composition is administered TID or QID'. Claims 9 and 10 depend from claim 1, wherein the recited composition 'comprises' a pharmaceutically acceptable carrier and an obesity relief agent consisting of ..... However, the specification as originally filed does not provide descriptive support for a composition comprising a pharmaceutically acceptable carrier and an amylin or an amylin agonist as recited being administered QID or TID. Page 30 of the originally filed specification describes 60 μg of pramlintide being administered TID or QID. The scope of the limitation: 'the composition comprising ... administered TID or QID' that is effective to treat obesity is not the same as the pramlintide species, amylin agonist or amylin being administered TID or QID that is effective to treat obesity. The QID or TID administered composition 'comprising' allows the presence of other element(s) in said composition such as an anti-diabetic agent, insulin, a gastric emptying-inhibiting agent etc. and lacks descriptive support in the specification, as originally filed. Therefore, the above-identified limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

42) Claims 1, 7 and 16 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1, as amended, includes the limitations: 'in need thereof, said method consisting of' administering to said subject an effective amount of a composition comprising an obesity relief

agent consisting of an amylin or an amylin agonist and a pharmaceutically acceptable carrier, 'wherein said amount is effective to treat obesity'. Claim 7, as amended, includes the limitations: a composition comprising 'an obesity relief agent consisting of' an amylin or an amylin agonist 'and a pharmaceutically acceptable carrier, wherein said amount is' effective to treat obesity. Claim 16, as amended, includes the limitation: 'in need thereof' comprising administering to said subject an effective amount of a composition consisting essentially of an amylin or an amylin agonist, 'wherein said amount' of the composition 'is effective to treat obesity'. Applicants point to the abstract and 8-9 at page 9 of the substitute specification for support to these amendments. However, the abstract of the instant application and lines 8-9 at page 9 of the substitute specification do not describe a method of treating obesity in a human subject in need thereof, said method 'consisting of' administering to said subject an effective amount of 'a composition comprising an obesity relief agent consisting of an amylin or an amylin agonist and a pharmaceutically acceptable carrier' as recited in the amended claim 1. These parts of the specification make no mention of 'a composition comprising' or 'a composition consisting essentially of' an amylin or amylin agonist in an amount that is effective to treat obesity, let alone a method 'consisting of' or 'comprising' administering such a composition to a 'human subject in need thereof' to treat obesity. The originally claimed six claims did not include the step of administering any 'composition' comprising, consisting of, or consisting essentially of an amylin, amylin agonist, or an amylin agonist analogue. The originally filed specification at pages 30-31 and Table I describes a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of one specific effective amount, i.e., 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type II diabetic subjects for four weeks, wherein said pramlintide administration was accompanied with the continued use of insulin. The method as described in the originally filed specification comprised insulin treatment *and* the administration of a specific dose of pramlintide to type II diabetic patients. This however does not provide descriptive support for the now claimed method of treating obesity in a human in need thereof, said method 'consisting' of administering to said subject an effective amount of a composition comprising an obesity relief agent consisting of any generic amylin or any amylin agonist and a pharmaceutically acceptable carrier, wherein said amount of the composition is effective to treat obesity. The scope of the limitation: 'amount of a

composition comprising ...' or 'amount of a composition consisting essentially of ...' that is effective to treat obesity is not the same as the 'amount of an amylin or amylin agonist' that is effective to treat obesity. The former limitation allows the presence of other element(s) in said composition such as an anti-diabetic agent, insulin, a gastric emptying-inhibiting agent etc. and lacks descriptive support in the specification, as originally filed. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Scope of Enablement)

43) Claims 1-7 and 9-17 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method of reducing the body weight of type 2 diabetic human subjects having a body weight not varying more than 45% from the desirable weight who have been on insulin treatment, within 15 minutes of each meal three times a day, to each said subject, 60 micrograms QID or TID of an amylin agonist which is ^{25,28,29}Pro-h-amylin (SEQ ID NO: 1), i.e., pramlintide, wherein said pramlintide is not administered in conjunction with another obesity relief agent, and wherein the mean body weight of said human subjects is significantly reduced after four weeks of said treatment compared to the mean body weight of said subjects prior to said treatment, does not reasonably provide enablement for a method of treating obesity in any human subject including a non-diabetic or a non-type 2 diabetic human subject in need thereof, or a type 2 diabetic human subject in need thereof who is not on insulin therapy, comprising administering any 'amylin', any 'amylin agonist', or any 'amylin agonist analogue' other than pramlintide, by any route other than "subcutaneous" route, and in any amount other than "60" micrograms TID or QID, as claimed in a broad sense. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected,

to use the invention commensurate in scope with the claims.

Instant claims are evaluated based on *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant application, the nature of the invention is treatment of obesity in a human subject in need thereof by administering an amylin, an amylin agonist, or an amylin agonist analogue in an amount effective to treat obesity. As described in the instant specification, the state of the art indicates that obesity or adiposity is a 'chronic disease that is highly prevalent in modern society' which is strongly associated with multiple conditions including diabetes mellitus, insulin resistance, hypertension etc. The step recited for example in claims 1 and 2 'consists of' administering to a human subject in need thereof an amount of a composition comprising a pharmaceutically acceptable carrier and an obesity relief agent consisting of an amylin, an amylin agonist, or an amylin agonist analogue in an amount effective to treat obesity. A method of treatment 'consisting of' such an administration step excludes insulin administration simultaneously, or minutes or hours before or after the administration. The method of treating obesity in a human subject in need thereof as claimed in the independent claim 7 'comprises' administering to said subject an amount of a composition comprising a pharmaceutically acceptable carrier and an obesity relief agent consisting of an amylin or an amylin agonist in an amount that is effective to treat obesity. The method of treating obesity in a human subject in need thereof as claimed in the independent claim 14 'comprises' administering to said subject a compound selected from the group consisting of an amylin, an amylin agonist, and pharmaceutically acceptable salts thereof, wherein the compound is administered in an amount effective to treat obesity and wherein said compound is not administered in conjunction with another obesity relief agent. What amount of 'pharmaceutically acceptable salts' of an amylin or amylin agonist qualifies as 'an amount effective to treat obesity' is not taught.

The method of treating obesity in a human subject in need thereof as claimed in the independent claim 16 'comprises' administering to said subject an effective amount of a 'composition consisting essentially of an amylin or an amylin agonist, wherein said amount' of the composition is effective to treat obesity. What amount of 'a composition consisting essentially of an amylin or an amylin agonist' qualifies as 'an amount effective to treat obesity' is not taught. The limitation in the claims 'an amount effective to treat obesity' as recited currently is not required to be an amount that is effective to treat obesity --in said human subject in need thereof--, but encompasses 'an amount effective to treat obesity' in a non-human and a human who is not in need thereof. The instant disclosure lacks a specific description for the limitation 'a composition consisting essentially of an amylin or an amylin agonist' as to what it excludes or includes, and therefore one cannot envisage whether or not the composition includes or excludes an element such as insulin, glucagons, or an anti-diabetic agent. The limitation 'a human subject in need thereof' encompasses moderately obese, morbidly obese, diabetic and non-diabetic obese, insulin-requiring and insulin non-requiring obese human subject as well as a human subject with age-associated obesity. The limitations "amylin agonist" and "amylin agonist analogue" broadly encompass a myriad of compounds, including a peptide and a nonpeptide compound (see paragraph bridging pages 13 and 14 of the original specification), non-human amylins, amylins having amino acid modifications or substitutions, and the art-accepted amylin agonists such as calcitonin and CGRP (see lines 45-47 in column 7 of US patent 5,739,106 and claims 3 and 10 of US 5,175,145, both already of record) etc. The breadth of the limitation 'obesity' encompasses non-diabetes-associated obesity, obesity associated with family genetics, morbid and non-morbid obesity, aging-associated obesity, insulin non-treated obesity, obesity due to hypernutrition etc. The limitation 'administering' in the independent claims encompasses administration by any route, i.e., intramuscular, intravenous, oral, intranasal, mucosal, topical, transdermal, transcutaneous etc. and non-mealtime administration, for example, administration 2-3 hours before or after each meal. Example 1 of the instant specification is limited to a demonstration that the human subjects of the study are those with a history of type 2 diabetes mellitus, who required insulin treatment for at least 6 months prior to the pre-screening visit. Body weight-wise, i.e., obesity-wise, these patients are described as having a body weight not varying more than 45% from the 'desirable weight' before admission into the study based upon

Metropolitan Life Tables. The only amylin agonist analogue that was administered in the instant invention was ^{25,28,29}Pro-h-amylin (SEQ ID NO: 1), also known as pramlintide. Groups of 'patients' were given separate mealtime pramlintide, 30 micrograms QID; 60 micrograms QID, or 60 micrograms TID subcutaneously before 15 minutes of each meal three to four times a day. Patients *remained on their insulin*, usual diet, and exercise regimens. The study period was limited to four weeks, i.e., 28 days, and the outcome was determined by comparing the mean body weight of the treated diabetic subjects with the mean body weight of the subject prior to the treatment. Thus, the originally filed specification at pages 30-31 and Table I describes a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of one specific effective amount, i.e., 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type 2 diabetic subjects for four weeks, wherein said pramlintide administration was accompanied with the continued use of insulin. The method as described in the originally filed specification thus comprised insulin treatment *and* the administration of a specific dose of pramlintide in type 2 diabetic patients. This decrease in body weight was statistically significant compared to the body weight of those type 2 diabetes patients who were treated with insulin alone. Table I demonstrates that 30 micrograms QID of pramlintide administered to insulin-taking type 2 diabetic subjects for four weeks did *not* induce a similar statistically significant or clinically meaningful reduction in the mean baseline weight of said subjects after week four. A statistically significant weight reduction from baseline to week 4 was observed in the patient group administered either with 60 micrograms TID (three times a day) or 60 micrograms QID (four times a day) pramlintide. There is no showing however that administration of any amount of pramlintide, let alone any other amylin agonist or amylin, administered 1 or 2 times a day did indeed induce obesity relief in diabetic or non-diabetic subjects in need of the treatment. This is evidence that the instant specification is enabling for a method of reducing body weight in a diabetic human patient with a history of type 2 diabetes mellitus who is on *continued insulin therapy*, comprising administering to the patient a specific amount, i.e., 60 micrograms QID or TID of a specific amylin agonist, i.e., pramlintide or $^{25, 28, 29}$pro-h-amylin, three or four times a day, via a specific route, i.e., subcutaneous route. However, the instantly claimed method in not enabled beyond this scope. This is critically important because there is no predictability that if one extrapolated the method of

reducing body weight in type 2 diabetic subjects to non-diabetic obese human subjects, obese subjects not on insulin treatment, or morbidly obese human subjects who are on or not on insulin therapy, the administered amylin, amylin agonist, or amylin agonist analogue including pramlintide, would bring about significant or clinically meaningful weight reducing or obesity-relieving effects. Neither the state of the art at the time of the invention, nor the instant specification as originally filed, provides specific guidance with regard to the use of a generic amylin, or a non-pramlintide amylin agonist, or a non-pramlintide amylin agonist analogue and its amount that is effective to treat obesity in any human subject in need thereof including an insulin-taking type 2 diabetic human subject. It should be noted that predictability or unpredictability is one of the *Wands* factors to be considered for enablement or lack thereof under 35 U.S.C § 112, first paragraph. Amylin, amylin agonist except pramlintide, and pharmaceutically acceptable salts thereof, are not enabled as obesity relief agents in the instantly claimed method. With regard to the therapeutic use of amylin, the state of the art indicates the difficulty, the undesirable pharmacological properties, and the impracticability of using amylin, including human amylin, clinically as 'a therapeutic agent'. For instance, Baron *et al.* (*Current Drug Targets – Immune, Endocrine & Metabolic Disorders* 2(1): 63-82, 2002) taught the following with regard to the clinical use of amylin as a therapeutic agent:

> Clinical use of amylin as a therapeutic agent is considered impractical because of its instability in solution and its propensity to aggregate and adhere to surfaces, properties that hamper the manufacturing, formulation, and storage of this peptide as a drug. Pramlintide is a synthetic, equipotent analogue of human amylin in which the undesirable pharmacological properties of human amylin (insolubility, tendency to self-aggregate) have been overcome by replacement of the three amino acid residues .... with prolines ....

Ratner *et al.* (*Diabetes Technol. Ther.* 4: 51-61, 2002) provide a similar teaching (see paragraph bridging the two columns on page 52):

> Native human amylin is not ideal for clinical use because of the peptide's poor solubility and propensity to aggregate.

Furthermore, with regard to the state of the art at the time of the invention, it should be noted that Applicants have previously argued the following (see pages 9, 13 and 14 of Applicants' Appeal Brief filed July 2000) [Emphasis in original]:

> .... THE RINK PATENT PROVIDES THAT AMYLIN AND AMYLIN AGONISTS ADMINISTERED AS DESCRIBED AND CLAIMED IN THE PRESENT APPLICATION HAVE "NO MEASURABLE EFFECT" ON FOOD INTAKE.
>
> .... the Rink patent reports that a 1.0 μg/kg dose (equivalent to about 70μg/dose in an adult human) had no effect on food intake.

The Rink patent that is being referred to by Applicants in the Appeal Brief is US 5,739,106 (already of record). Applicants have not shown within the instant specification that human or non-human amylin or a composition comprising, consisting of, or consisting essentially of the same, was in fact stable, soluble and/or non-aggregating enough to be therapeutic in a method of treating obesity upon administration in any amount and by any route, with or without concurrent insulin therapy, to a human subject in need thereof. How to determine an amount that is effective to treat obesity of a compound that is recognized in the art to be insoluble and self-aggregating is not taught. A method of treating obesity in non-diabetic human subjects or subjects not on insulin therapy consisting of or comprising administering an amylin, amylin agonist, or an amylin agonist analogue including pramlintide, or a composition consisting essentially of or comprising of the same, is not enabled. This is important because there is no predictability that if one of skill in the art administered a human or non-human amylin, amylin agonist, or an amylin agonist analogue including pramlintide, or a composition comprising or consisting of the same, to a non-type II diabetic obese human not on insulin therapy, in an amount taught within the instant specification, the administered amylin, amylin agonist, an amylin agonist analogue, or pramlintide, would bring about a therapeutic effect against obesity in said subjects. With specific reference to pramlintide, the state of the art several years after the effective filing date of the instant application, documents that the weight effect of pramlintide in non-insulin treated human subjects is not known. For instance, Hollander *et al.* (*Obesity Res.* 12: 661-668, April 2004) documents the following (see page 666) [Emphasis added]:

> Studies in non-insulin-treated subjects **would allow** examination of the weight effect of pramlintide without the potential confounding effect of changes in insulin use.

The weight reducing or obesity-relieving effect of pramlintide administered alone or as an adjunct to insulin therapy, to a non-diabetic human patient, or the weight reducing or obesity-relieving effect of any amylin, amylin agonist, or amylin agonist analogue, administered alone or as an adjunct to insulin therapy, to an obese diabetic or non-diabetic human subject, is simply not predictable. For the reasons delineated above and due to the lack of specific direction or guidance within the instant specification, the breadth of the claims, the absence of working examples enabling the full scope, the art-recognized unpredictability factor, and the quantity of the experimentation necessary, a

considerable amount of undue experimentation would have been required to reproducibly practice the full scope of the invention, as claimed. Instant claims do not meet the scope of enablement provisions of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

44) Claims 1-7 and 9-17 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 6 is vague, indefinite and confusing in the limitation: "said amylin or amylin agonist is administered in an amount from .....". Claim 6 depends from claim 5, which in turn depends from claim 1. Claims 5 and 1 recite that what is administered in an amount effective to treat obesity is the recited 'composition'. However, the dependent claim 6 recites that 'said amylin or amylin agonist is administered in an amount from .....'. Does it mean that the amylin or the amylin agonist that is administered in the method of claim 6 is in addition to the composition administered in claim 5 or 1?

(b) Analogous rejections and criticism apply to claims 11-13.

(c) Claim 10 is vague, indefinite, incorrect and inconsistent with the claim language used in claim 9 in the limitation: 'is administered TID or QID contains'. For the purpose of distinctly claming the subject matter, it is suggested that Applicants replace the above-identified limitation with the limitation --is administered TID or QID and contains--.

(d) Claims 1, 7, 14 and 16 are vague and indefinite in the limitation: 'amount effective to treat obesity' because it is unclear in whom the recited amount is effective to treat obesity. For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the above-identified limitation with the limitation --amount effective to treat obesity in said human subject--.

(e) Claims 2-6, 9-13, 15 and 17, which depend directly or indirectly from claim 1, 7, 14 or 16, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

45) Claims 1-7, 9-14, 16 and 17 are rejected under 35 U.S.C § 102(a) as being anticipated by

Kolterman *et al.* (WO 96/40220, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

It is noted that the inventorship of the Kolterman ('220) publication (Kolterman, Thompson, and Mullane) is non-identical with the inventorship of the instant application (Duft and Kolterman). Therefore, the publication of Kolterman *et al.* ('220) is proper prior art under 35 U.S.C. § 102(a). See MPEP 2132 III.

It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification. It is noted that the patient population used in the instant invention to treat obesity by the administration of the recited amount of pramlintide is insulin-requiring Type 2 diabetics. See Example 1 of the instant specification.

Kolterman *et al.* ('220) taught a method of administering to an insulin-taking type II diabetic human subject a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137 (i.e., SEQ ID NO: 1). The composition consists of pramlintide and a pharmaceutically acceptable carrier, and is administered in single or multiple doses, for example, in a dose of about 30 micrograms QID or about 60 micrograms TID or QID. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph in page 19; lines 8-10 on page 19; and first row reciting 'Insulin-Treated Patients' in each Table. Pramlintide is administered subcutaneously 1-4 times a day before meals (see pages 9 and 22). Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus' (see page 10). Kolterman *et al.* ('220) taught the benefit of obtaining weight loss in Type II diabetic patients by teaching that hyperglycemia associated with Type II diabetes can be reversed or ameliorated by weight loss sufficient to restore the sensitivity of the peripheral tissues to insulin (see pages 7, first paragraph), thus indicating that Type II diabetic patients are in need of weight loss. Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient population

used by Applicants in Example 1 of the instant application. The prior art method is the *same* as the instantly claimed method in terms of the amylin agonist or the amylin agonist analogue (pramlintide), the amylin agonist composition, or the amylin agonist analogue composition administered, and the insulin-taking Type II diabetic patient population used, 80-90% of whom are known in the art to be intrinsically obese as taught by Tsanev (see Tsanev's abstract), the subcutaneous route of administration, the dose and the daily frequency of the amylin agonist administered, and the administration step prior to meals. Given Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinsically obese, and given Kolterman's ('220) express teaching that obesity is a characteristic of 'most patients with Type II diabetes mellitus', Kolterman's ('220) method of subcutaneous administration of pramlintide to Type II diabetic patients in an amount that falls within the range recited in the instant claims necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method. Kolterman's ('220) type II diabetic patients to whom pramlintide composition is administered necessarily qualify as human subjects 'in need thereof' as recited in the instant claims. Since the structural limitations of the instantly claimed method are clearly met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the same therapeutic effect. The Office's position that Kolterman's ('220) method is the same as the Applicants' claimed method is based upon the fact that the method step, the compound administered, the amount of the compound administered, the route by which the compound is administered, and the intrinsically obese diabetic human patient population to which the compound is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese type 2 diabetic human subjects anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about a therapeutic effect against the intrinsic obesity in the pramlintide-treated type II diabetic patients as defined in the instant invention, i.e., by controlling body weight for cosmetic purposes, or by improving bodily appearance in the diabetic patients.

Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 1-7, 9-14, 16 and 17 are anticipated by Kolterman *et al.* ('220). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* ('220), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* ('220), with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of 80-90% of obesity in the diabetic subjects, is necessarily present in the thing described by Kolterman *et al.* ('220).

46) Claims 7, 14, 16 and 17 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al.* (US 5,686,411, already of record) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

The limitation 'consisting essentially of' in claim 16 and the limitation 'method ... comprising ..... wherein said compound is not administered in conjunction with another obesity relief agent' in claim 14 do not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent, etc. in the recited composition.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor

of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Gaeta *et al.* ('411) taught a method of treatment of diabetes mellitus in a mammal, including a patient seen by a medical practitioner, i.e., a human, comprising the administration to said mammal of a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1). See claims 34, 35 and 19; and lines 45-53 in column 7 of the '411. Gaeta *et al.* ('411) taught the 'therapeutically effective amount' of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls in the range of therapeutically effective amount of the amylin agonist disclosed in the '411 patent. The portion of the disclosure of the U.S. patent '411 at lines 9-14 of column 3 describes that the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus and that the administration is of amylin agonist analogue *alone*. The amylin agonist composition comprises a pharmaceutical carrier and the amylin agonist without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least 80-90% of the diabetic patients used in the method disclosed in the '411 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '411 patent comprising the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist ^{25,28,29}Pro-human amylin to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims and the amount administered are the same, the method of the '411 patent is expected to bring about a therapeutic effect against intrinsic obesity in Gaeta's ('411) treated diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

Claims 7, 14, 16 and 17 are anticipated by Gaeta *et al.* ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta *et al.* with

the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of 80-90% of obesity in the diabetic subjects, is necessarily present in the thing described by Gaeta *et al.* ('411).

47) Claims 1-7, 9, 11-14, 16 and 17 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000).

It is noted that a 70 kg patient is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. The human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 79 kg. For example, the recited therapeutic amount range of 'about 0.1 milligrams per day to about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to about 5 mg/day of the amylin agonist or amylin agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See lines 4-8 of page 23 of the substitute specification; and paragraph bridging pages 23 and 24 and lines 3-7 on page 24 of Applicants' response filed December 2002. It is particularly noted that the mean body weight $\pm$ SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg diabetic patients from Kolterman's (1996) study qualify as 'human subjects in need thereof' as recited in the instant claims.

It is noted that the claimed method of treating obesity in a human subject in need thereof encompasses alleviating the 'symptoms' of the disorder, i.e., obesity. See the last paragraph on page 9 of the substitute specification. The substitute specification at paragraph bridging pages 7 and 8 characterizes 'increased appetite' as a sign strongly associated with obesity (see second paragraph). Thus, increased appetite and therefore, increased food intake is viewed as a 'symptom' of obesity. It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or

complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification.

Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide is administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg diabetic patients from Kolterman's (1996) study qualify as 'human subjects in need thereof' as recited in the instant claims. Additionally, even BMI-wise, Kolterman's (1996) diabetic subjects meet the limitation 'human subjects in need thereof' as recited in the instant claims, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27 (see second full paragraph under 'Subjects, materials and methods). Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as obese diabetic subjects in light of what is known in the art. For example, Itasaka *et al.* teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans (see abstract of Itasaka *et al.*). Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent, but consisted of or consisted essentially of pramlintide. The pramlintide composition was injected subcutaneously to the human patients (see 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms three times a day to 'about 0.1 milligrams' or 300 micrograms per day. See 'Study design'; Table 1; and paragraph there below. Kolterman's (1996) subcutaneous administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to diabetic human subjects weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27 anticipates the instant claims. Thus, the very active step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al.* in April, 1996. Given that the method step in Kolterman's (1996) method and the instant claims are the *same* and the amount administered are

the *same*, Kolterman's (1996) method is expected to necessarily bring about the same therapeutic effect in the pramlintide-treated diabetic patients as defined in the instant invention, i.e., by controlling body weight for cosmetic purposes, or by improving bodily appearance in the diabetic patients. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable. Irrespective of the mechanism(s) of action of the amylin agonist pramlintide and irrespective of whether amylin is a peripherally or centrally acting agent, whether or not pramlintide is an anorectogenic agent, gastric emptying-delaying agent, or a food intake suppressing agent, the prior art method of administering the above-explained amount of the amylin agonist ^{25,28,29}Pro-human amylin (pramlintide or SEQ ID NO: 1) to diabetic human subjects weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 necessarily serves as the Applicants' method of treating obesity as defined in the instant application, i.e., 'controlling weight for cosmetic purposes ..., that is to control body weight to improve bodily appearance' in said diabetic human subjects.

Claims 1-7, 9, 11-14, 16 and 17 are anticipated by Kolterman *et al.* (1996).

48) Claims 7, 14 and 16 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008, already of record) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

The limitation in claim 16: 'a composition consisting essentially of an amylin or an amylin agonist' and the limitation in claim 14: 'method ... comprising ..... wherein said compound is not administered in conjunction with another obesity relief agent' does not exclude the administration

of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent such as exendin etc. It is further noted that 'amylin agonist' is defined in the instant specification as a peptide or non-peptide compound that mimics the effect of amylin. See paragraph bridging pages 13 and 14 of the originally filed specification. Calcitonin and CGRP are described in the instant specification as sharing the food intake-suppressing action or effect of peripherally or centrally administered amylin. See paragraph bridging pages 9 and 10 of the originally filed specification.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Beumont *et al.* ('008) taught a method of treating diabetes mellitus in an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus comprising the subcutaneous administration to said human of a therapeutically effective amount of an amylin agonist *alone* such as calcitonin, or calicitonin and insulin, contained in a pharmaceutically acceptable carrier. See claims 11, 7, 13 and 4; lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2. Claim 11 of the '008 patent is directed to the method of administering a therapeutically effective amount of the amylin agonist calcitonin to an insulin-requiring human with diabetes mellitus. The 'therapeutically effective amount' taught by Beumont *et al.* ('008) includes the typical dosage units of about 0.1 to 1 mg of calcitonin. See first full paragraph in column 13. The amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls in the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least 80-90% of the diabetic patients used in the method disclosed in the '008 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to diabetic humans

anticipates the instant claims. Given that the method step of the '008 patent and the instant claims and the amount administered are the same, the method of the '008 patent is expected to bring about a therapeutic effect against intrinsic obesity in Beumont's treated diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

Claims 7, 14 and 16 are anticipated by Beumont *et al.* ('008). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Beumont *et al.* ('008), but rather is used to show that every element of the claimed subject matter is disclosed by Beumont *et al.* ('008) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of 80-90% of obesity in the diabetic subjects, is necessarily present in the thing described by Beumont *et al.* ('008).

Relevant Art

49) The art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Newgard *et al.* (US 6,110,707, filed 01/17/1997) envisioned providing amylin to a mammal exhibiting pathologic obesity (see lines 41-46 in column 4).
- Kopelman (Editorial. *Internat. J. Obesity* 23: Suppl. 7, S1, 1999) taught the existence of a clear association between obesity and type 2 diabetes. Kopelman taught that the two conditions share many common aetiopathological features and 80% of patients with type 2 diabetes are obese. Kopelman taught that the logical way to address the problem would seem to be via an integrated weight management approach using pharmacotherapy. Kopelman taught that numerous studies have shown that losing 5-10% body weight leads to significant improvements in a wide range of metabolic parameters, thereby reducing the need for anti-diabetic medication. See left column.

Remarks

50) Claims 1-7 and 9-17 stand rejected.

51) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile

transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

52) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

53) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

February, 2007

S. DEVI, PH.D.
PRIMARY EXAMINER